ON THE

ssociation of Chronic Interstitial Nephritis with Pulmonary Tuberculosis.

(Thesis for M.D. Degree.)

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ON THE ASSOCIATION OF CHRONIC INTERSTITIAL NEPHRITIS WITH PULMONARY TUBERCULOSIS.

THE presence of albumen in the urine of cases of pulmonary phthisis is common, and the clinical significance varies according to the condition of the kidneys giving rise to it. It is, therefore, of great importance in each case to determine what the condition of the kidneys is.

A faint cloud of albumen may occur on testing the urine in cases of pulmonary phthisis, with much pyrexia, probably due to a condition of "cloudy swelling" in the kidneys, such as may occur in any case where there is prolonged or hectic fever, and possibly this condition may in some cases progress to one of actual parenchymatous nephritis. I have, however, on several occasions tested urines of phthisical patients in the Brompton Hospital, when they had much hectic fever, and even shortly before their death, and have failed to find a trace of albumen. Nevertheless, a trace of albumen may occasionally be found in cases where a subsequent *post-mortem* examination fails to detect anything abnormal in the kidneys.

However, in the majority of cases of pulmonary phthisis where on repeated examinations albumen is found to be present in the urine withous pus, I think one of the following two conditions is most frequently present, namely :—

(1) Lardaceous disease of the kidney ;
(2) Some degree of chronic interstitial nephritis.

The latter of these two complications I consider allows of the less unfavourable prognosis, and it is the association of this kind of kidney disease with pulmonary phthisis which I shall alone consider in this paper.

In looking at *post-mortem* examinations at St. Bartholomew's Hospital, I have been struck by the number of cases (including many on the surgical side) where quiescent, often calcareous, remains of tubercle at the apices of the lungs were associated with some degree of chronic interstitial nephritis. I wondered if there could be any causal connection between the two, and it is this point which I shall now consider.

Dr. Ormerod in 1890[1] tabulated a series of cases in which *post-mortem* examination showed the presence of quiescent or obsolete pulmonary phthisis. He found the frequency of chronic kidney disease (chiefly interstitial) amongst these cases to be greater than amongst 100 consecutive *post-mortem* cases of patients over 20 years old.

Even in the case of patients who have died of their pulmonary tuberculous disease, I think that there is evidence of chronic interstitial nephritis, if present, having exercised some modifying influence on the lung disease. From looking over the Brompton *post-mortem* books, it appears to me that there is usually more fibrosis associated with the tubercle in those cases where there is also chronic interstitial nephritis. This points to an increased healing tendency in such patients, even if they ultimately died from a fresh onset of pulmonary tubercle.

It may be added that many of those cases which succumbed to a fresh onset of pulmonary tuberculosis, had also laryngeal tubercle, a complication adverse to quiescence of the lung disease.

The evidence of quiescent or obsolete pulmonary tubercle varies considerably. It may consist of puckering of one or both apices by a dense fibrous material, and this fibrous material may have spots of caseous, sometimes partially calcified, substance enclosed in it. Sometimes there are one or two encapsuled calcareous nodules at one apex or both. Probably in many of these cases evidence of the condition in the lungs would have been very hard to obtain by physical signs during life, but this is not always the case—notably in one of the first cases I saw of this class, which I am allowed to quote by the kindness of Dr. Reginald Thompson. Here the physical signs pointed to the pulmonary phthisis being far advanced in the third degree, and at the *post-mortem* examination I was surprised to find how quiescent the whole tuberculous process really was.

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[1] Lecture at Victoria Park Hospital (printed in *Medical Press and Circular*, 10th September, 1890.)

H—— H——, 46; married; no children; book-keeper in a shop. Admitted into the Brompton Hospital 4th July, 1890, died 10th October, 1890.

Family History.—Father died at 62 of morbus cordis (had gout). Mother possibly died of phthisis. Two brothers died of phthisis. One brother living and well. Two sisters died of phthisis.

Previous History.—Discharged from the Royal Navy at 18 for "phthisis pulmonalis." Gout in left great toe at 31; has had four attacks of gout since, but he thinks never in any other joint. Since leaving the Navy had good health till five and a-half years ago.

Present Illness he dates from five and a-half years ago, when he says that he had some cough, worse at night-time, and occasionally spat up some black clotted blood. Since then has had cough and expectoration; has been losing flesh, but has had no night sweats lately; no diarrhœa.

On Admission.—Rather anæmic, sallow and wasted. *Chest:* some flattening of upper right front. *Heart:* A.B. not felt; sound faint; no murmur. *Lungs: Right:* impaired resonance over upper front with cavernous signs to second rib in front and to middle of infra-scapular region behind. Crepitations below second rib in front to fifth. *Left:* impaired resonance and crepitations over upper front. Moderate amount dry cough. Radial pulse, 96, regular; arteries thickened. Liver, not enlarged. Grating in metatarso-phalangeal joint of right great toe. Appetite bad. Bowels confined.

July 19th.—Gouty swelling about metacarpo-phalangeal joint of little finger of right hand.

July 28th.—Subacute gouty swelling in both big toes and right little toe.

Aug. 22nd.—Much vomiting lately independent of cough, slightly relieved by ½ cocaine lozenges (containing about $\frac{1}{6}$ gr. in each) before meals.

There was very little change in the lung signs; moderate cough; only a little expectoration (chiefly mucus); no more gout in the joints. Vomiting continued on and off. Patient's temper became very "grumpy" and melancholic. There was considerable wasting.

Urine, average about 40 oz. in the 24 hours, acid, pale clear, 1010 specific gravity; albumen usually $\frac{1}{7}$ to $\frac{1}{5}$; occasionally a few granular casts were found. The vomiting was probably due to chronic uraemia. No albuminuric retinitis found. Patient began to get drowsy on October 8th. On October 9th he could not apparently recognise his wife or say anything. On October 10th, eczema all over body; legs drawn up rigidly; knee jerks increased (especially on right side). Left facial paresis; no definite paralysis of limbs. Patient was constantly scratching himself. Twitchings of facial muscles very noticeable. Respiration about 20, rather shallow. Pulse 76, regular, small, rather low tension. Died on October 10th, at 12.30 p.m.

A *post-mortem* examination was made by Dr. R. Maguire on October 11th.

Brain.—Slightly congested, otherwise normal.

Lungs.—Old pleural adhesions at both apices. *Right Lung.*—Excessive pleural thickening over apex; on section in upper lobe many small caseous nodules, surrounded by fibrous tissue, and three small cavities in lower part of the lobe filled with caseous material, the walls composed of thick fibrous tissue; the whole of the upper lobe was much contracted; middle and lower lobes normal. *Left Lung.*—There were three lobes. Excess of fibrous tissue in upper lobe; small caseous nodule about the size of a filbert in the middle lobe; the lower lobe normal.

Heart.—Somewhat hypertrophied. All the valves were somewhat thickened, but were otherwise of normal structure.

Kidneys.—Normal size. On section, tough, and cortex diminished. Capsules peeled off easily but left a granular surface, on which were seen a few fatty spots, but no cysts.

Liver.—Normal in size and to section. Two gall stones in the gall bladder, one of them blocked the orifice of the cystic duct.

Spleen.—Slightly enlarged, firm on section.

Stomach
Pancreas
Duodenum
Intestines
Bladder
Larynx
Trachea
Pharynx
Œsophagus

Normal.
No amyloid reaction found in any of the viscera.

Joints.—5th right metacarpo-phalangeal joint was examined and urate of soda was seen deposited in the substance of the cartilage.

In this case by the physical signs I expected to find large cavities, and at least some active tubercle. At the *post-mortem* examination, however, no recent tubercle was found, but extreme fibrosis around the caseous remains from the tuberculous process. Death in this case was due to chronic uræmia with gouty kidneys.

In the cases of pulmonary tuberculosis, associated with some degree of chronic interstitial nephritis, the pulmonary disease usually runs a very chronic course or becomes quite quiescent or obsolete. In many of these cases probably the existence of pulmonary tubercle was never very evident during life, but in other cases the commencement may have been acute, as in the patient H——, notes of whose case I have just given (at 18 years old, I believe, it was supposed that he could live a very short time only). The expectoration is scanty usually and chiefly mucous. The collective symptoms may be rather those of emphysema than of tubercle of the lungs. The patients mostly live, I think, to past middle life, and death may be due to some quite independent cause, such as acute pneumonia or an accident coming under the notice of the surgeon, or death may be due to the renal disease, as in the case of the patient H——. To this general rule, however, I have seen already notable exceptions in which patients past middle life with chronic interstitial nephritis have succumbed to an acute onset or dissemination of pulmonary tubercle. In these cases, I think, laryngeal tuberculosis is usually found, a complication which terribly hinders the quiescence and healing process of pulmonary tuberculosis. This termination is probably also far more likely to occur in the broken-down subjects of chronic alcoholism, the relation of which to tuberculous processes was fully discussed in connection with Dr. Payne's paper before the Pathological Society, published in the *Transactions* of 1889.[1]

Phthisical patients, again, with chronic interstitial nephritis, in whom the pulmonary tuberculous process, though chronic, has not quite ceased, are probably more likely than patients without kidney disease to succumb to fatal hæmoptysis,[2] for the kidney disease increases the tendency to degeneration in the pulmonary as in the systemic arteries, and probably favours the formation of small pulmonary aneurisms, and the rupture of these often gives rise to fatal hæmoptysis.

To return now to the original question; it may be urged that the quiescence of pulmonary tubercle has nothing to do with the presence of chronic interstitial nephritis, but that the diseases belong to different periods of life, and that many of those phthisical patients who survive ultimately get kidney disease. To combat this objection I shall compare two series of *post-mortem* cases in both of which the subjects were past 40 years of age. In the first series are only cases of quiescent or obsolete tubercle, death occurring from some other cause. The second series consists of cases of pulmonary tubercle at the Brompton Hospital, in nearly all of which the pulmonary disease was the actual cause of death. Here, in spite of the caution as regards age, there will still be found a marked difference in the relative frequency of chronic interstitial nephritis in the two series; it being much more frequent in the first series than in the second.

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[1] *Trans. Path. Soc.*, vol. i., p. 333 et seq. See also the elaborate paper by Dr. W. H. Dickinson, *Trans. Med. Chir. Soc.*, 1873, vol. lvi., pp. 27 et seq.

[2] This, I think, also is confirmed by the Brompton *post-mortems*. In cases of fatal hæmoptysis, however, I believe, there is nearly always evidence at the *post-mortem* of the tuberculous process still going on in the lungs, although not necessarily very actively.

I first give a table of 29 cases of quiescent or healed phthisis from the medical *post-mortem* register of St. Bartholomew's Hospital, 1891, which were not used by Dr. Ormerod in his paper. Total 29 cases. Let us leave out Nos. 11 and 28 with congenital abnormality of kidneys and accept the other 27 cases. Of these there are 20 (including the two cases where there had probably been tubercle at apices) over 40 years old and of these 11 had, I consider some amount of chronic interstitial nephritis.

Amongst Dr. Ormerod's[1] 50 cases of healed or quiescent phthisis, there are 24 of patients over 40 years old in which the condition of the kidneys is definitely stated. Of these I should say that 16 had chronic interstitial nephritis (in varying degree) and 8 had not interstitial nephritis. Adding these 24 cases of Dr. Ormerod to the 20 cases mentioned above, we get a total of 44 cases of healed or quiescent phthisis in patients over 40 years old; of whom 27 had chronic interstitial nephritis against 17 who had not, *i.e.*, 61.3 per cent. were instances of chronic interstitial nephritis in cases of healed or quiescent phthisis over 40 years of age.

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[1] Quoted already.

Analysis of Quiescent and Healed Phthisis from Post-Mortem (Medical Side) Book, 1891 (with kind permission of Dr. Norman Moore and Dr. Ormerod).

No.	Sex and Age.	Evidence of old Phthisis	Cause of Death.	Kidneys and Remarks.
1	F. 58	Good	Malignant disease of peritoneum	Interstitial.
2	M. 39	Good	Acute pneumonia	Capsule adherent.
3	M. 38	Good	Pneumonia, &c.	Interstitial.
4	M. 39	Scarred apex	Aneurysm ruptured (aortic)	Natural.
5	M. 45	Good	Pericarditis, &c.	Interstitial.
6	M. 51	Good	Delirium tremens	Natural.
7	M. 35	Probable	Aneurysm of aorta ruptured	Natural.
8	M. 58	Good	Bronchitis and emphysema	Interstitial (and gout).
9	M. 43	Good	Chronic peritonitis, &c.	Natural (gout).
10	M. 69	Good	Bronchitis and emphysema	Capsule adherent.
11	M. 32	Good	Delirium tremens	One kidney absent (congenital).
12	M. 19	Good	Double pneumonia	Natural.
13	M. 44	Good	Pneumonia	Interstitial (and gout).
14	M. 67	Probable	Cerebral hæmorrhage	Interstitial.
15	F. 34	Good	Morbus cordis	Interstitial.
16	M. 57	Probable	Pneumonia	Natural.
17	M. 45	Good	Cerebral hæmorrhage	Interstitial (probably also gout).
18	M. 50	Good	Morbus cordis	Interstitial (and gout).
19	M. 55	Good	Intestinal cancer	Natural.
20	F. 50	Good	? (brought in dying)	Interstitial (and gout).
21	F. 52	Good	Morbus cordis	Natural.
22	M. about 40	Good	? (brought in dead)	Probably interstitial.
23	F. 47	Good	Œdema glottidis, probably syphilitic disease of larynx	Natural.
24	M. 50	Good	Cancer of pancreas	Natural.
25	M. 60	Good	Dilatation of whole œsophagus with scar at cardiac orifice of stomach—gastric atrophy? starvation	Natural?
26	M. 46	Good	Pericarditis	Interstitial (gout).
27	F. 47	Good	Morbus cordis	Natural.
28	M. 50	?	Cerebral hæmorrhage	Congenitally small.
29	M. 37	?	Pneumonia	Natural.

For the second series I was kindly permitted to make use of the *post-mortem* book at the Brompton Hospital and found amongst 145 *post mortems* on patients with pulmonary tubercle over 40 years old, nearly all of whom actually died of their lung disease, that there was some degree of chronic interstitial nephritis in 58 cases, and none in 87. I found therefore evidence of chronic interstitial nephritis in 40 per cent. of the cases only, whereas in the first series there was evidence in 61 per cent. of the cases.[1]

Although I cannot yet consider my point proved, still I hope that I have made it seem probable that there is a causal relation between chronic interstitial nephritis and the quiescence of pulmonary tubercle, and that this relation exists independently of the age of the patient, I shall now, therefore, proceed to some points which might have a bearing on this relation. First, there is the question of the influence of gout.

It has been suggested that it is gout in these cases which arrests the tuberculous process in the lungs and renders the phthisis quiescent. Unfortunately, hitherto, at *post-mortems* the great toe and other joints have not been systematically examined for the presence of urate of soda,[2] hence the existence of gout in these cases has not been recorded. It has long been supposed that gout or the gouty diathesis is antagonistic to phthisis (vide Sir Dyce Duckworth's book on "Gout").

It may be urged that the inherited diathesis, which favours the development of gout, proves also antagonistic to the development of tubercle. Against this view are some notable examples where phthisical patients became gouty, and their lung disease, though acute at first, became chronic or even quiescent.

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[1] I have also endeavoured to find out the frequency of chronic interstitial nephritis amongst those that die past 40 years of age and do not die of pulmonary tuberculous phthisis. Out of 838 cases from St. Bartholomew's medical *post-mortem* book 378 showed some degree of chronic interstitial nephritis, *i.e.*, 45.1 per cent. This percentage occupies an intermediate place between the two given above, and therefore tends to confirm them. Throughout I have endeavoured to include all the minor degrees of chronic interstitial nephritis, and hence perhaps the percentage seems high in all three series.

[2] In some cases of quiescent pulmonary tubercle, where the urate was looked for, it was certainly not present; in some other cases there was evidence of gout at the *post-mortem*, when the kidneys showed no sign of chronic interstitial nephritis.

The case of the patient Hudson already narrated is a good example. Here a man with family history of both gout and phthisis suffered severely from phthisis in early life. Later on the pulmonary disease became quiescent with onset of the gout; he developed a gouty kidney which ultimately killed him. In such cases, perhaps, the excessive fibrosis may act as a mechanical barrier, hindering the spread of tubercle in the lungs.

What influence can alcohol have? Can the taking of alcohol exert both an antagonistic action to the tubercle and produce chronic interstitial nephritis? That this is not the case, I think, is shown by the following facts:—

(1) Chronic interstitial nephritis is of comparatively infrequent occurrence in *post-mortems* on cases of cirrhosis of the liver,[1] and it has been experimentally demonstrated that only a small percentage at most of the alcohol taken is excreted by the kidney[2] before oxidation in the body.

(2) Apparently there is a disposition to tubercle in the subjects[3] of alcoholism. On the other hand, the taking of alcohol, at all events in England, may favour the development of gout and gouty kidney.

Although almost every drug has been tried in cases of phthisis and numberless experiments have been made on animals, I am not aware that substances like uric acid, etc., have ever been injected into the blood or the subcutaneous tissues of animals before or after inoculation with tubercle. Yet it may just occur to one that there might be some substance circulating in the blood in cases of gout, in minute quantities, yet sufficient to have an antagonistic action to the growth of the tubercle in the body; and there might be the same substance in other diseases such as chronic interstitial nephritis, and perhaps in people taking an unusual amount of food. This latter might partly account for the good result following the extra feeding of phthisical patients when duly assisted by hygienic influences. It is, however, premature to do more than suggest the possibility of such associations, since I have not quite succeeded in proving any causal connection between quiescent tubercle and chronic interstitial nephritis, although at all events I hope that I have made such a connection seem probable. To make it seem more than probable, I hope ultimately to have opportunity for gathering more facts.

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[1] *Vide* Dr. Payne's paper and discussion, *Path. Soc. Trans.*, 1889, vol. xi., pp. 333, et seq., and Dr. Dickinson (already quoted).

[2] *Vide* paper by C. Binz in *Archiv. für Experimentelle Pathologie*, Leipzig, 1877, vol. vi., pp. 287, &c. (Also later address at 7th German Med. Congress, Wiesbaden (1888). He finds that from nothing to a little over 3 per cent. of the total alcohol taken, may be got rid of by the kidneys; and that nothing or a mere trace is excreted by the lungs.

[3] *Vide* Dr. Payne's paper again. After middle life the occurrence of phthisis seems to become more frequent in the intemperate than in the temperate. Dr. Walshe and older writers probably followed the Registrar General's Reports for which causes of death in inn-keepers, potmen, &c., were often certified without *post-mortem* examination. See also Dr. Dickinson's paper, *Med. Chir. Soc. Trans.*, 1873, vol. lvi., pp. 27, et seq.

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